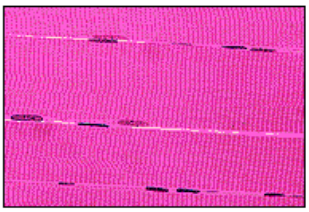
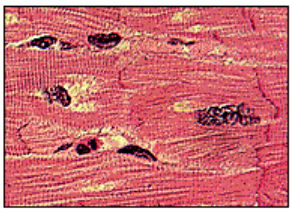
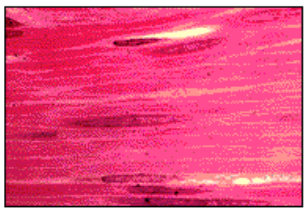
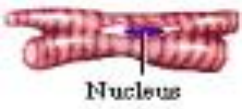
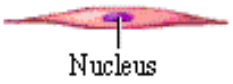
# Introduction

- Muscles are specialized tissues for contraction and force generation.
- There are three types of muscle tissues in the body:
  1- Skeletal muscles
  2- Cardiac muscles
  3- Smooth muscles
- These muscle tissues differ in their body location, their shape, structure of their cells, and the means by which they are activated to contract.

## Comparison between Skeletal, Cardiac & Smooth muscle cells:

| | **Skeletal** | **Cardiac** | **Smooth** |
|---|---|---|---|
| |  |  |  |
| **Site** | Attached to the skeleton | Found only in the heart | Found in the wall of hollow visceral organs |
| **Cell Shape** |   Elongated |   Elongated |   Spindle shape |
| **Nuclei** | Multiple peripheral nuclei | Central single nuclei | Single central nuclei |
| **Visible Striation** | + | + | No striation |
| **Control** | Voluntary | Involuntary | Involuntary |
| **Function** | - Maintain posture<br>- Voluntary movements | Pumping of the blood | Regulate flow of materials though the hollow visceral organs |

# Smooth Muscle

## Introduction:

- Smooth muscle shares some basic properties with skeletal muscle, but it also displays a unique contractile characteristics.
- Smooth muscle has a specialized contractile apparatus made up of thin actin filaments that slide relative to stationary thick myosin filaments in response to a rise in cytosolic $Ca^{2+}$ to accomplish contraction.
- Also, it is directly use ATP as the energy source for cross-bridge cycling.
- However, the structure and organization of fibers within the muscle vary, as do the mechanism of excitation and the means by which excitation and contraction are coupled.
- Furthermore, important distinctions occur in the contractile response itself.

## Functional Structure of Smooth Muscle Cell:

- A smooth muscle cell is spindle shaped (tapered at both ends), with single central nucleus.
- It contains the contractile proteins actin and myosin, the regulatory protein *calmodulin*.
- Smooth muscle contractile proteins are not arranged in regular arrays with *no striations*.
- Instead of Z lines, there are *dense bodies* in the cytoplasm located throughout the cell. Some of these dense bodies are attached to the cell membrane; whereas others are held in place by a structural protein that cross-attache from one dense body to another.
- Large number of actin filaments is attached to the dense bodies and there is no sarcomere.
- Its sarcoplasm contains *poorly developed sarcoplasmic reticulum* and no T-tubules.
- It also contains *few mitochondria* and it depends to a large extent on glycolysis for their metabolic needs.
- Smooth muscle is *under involuntary control*; it receives autonomic nerves that modulate its activity.

## Types of Smooth Muscles:

I- Single-unit smooth muscle:

**Site**:

- In the walls of hollow visceral organs e.g. GIT, urinary bladder and uterus.
- It is also called "visceral smooth muscle" or "unitary smooth muscle".

**Cell**s:

- They collect into sheets or bundles.

- They are connected by gap junctions (functional syncytium = syncytial smooth muscle) → obeys the "*all or none law*".
- They have unstable RMP with spontaneous electrical activity.

**Contraction**:

- Single-unit smooth muscle is self-excitable, so it does not require nervous stimulation for contraction.
- They can develop spontaneous contractions (= myogenic) & contract together as a single unit.

## II- Multi-unit smooth muscle:

**Site**:

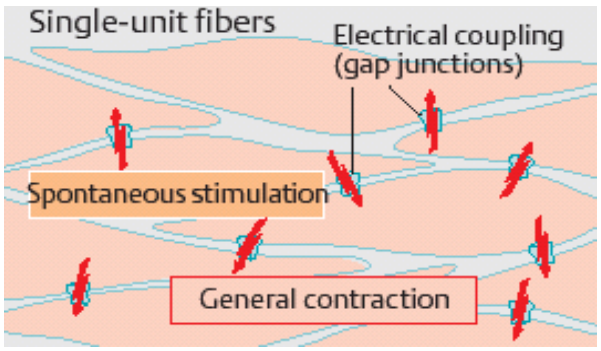
- Discrete muscle (= separate) fibers present in the ciliary muscle, iris of the eye, and piloerector muscle of the hair.

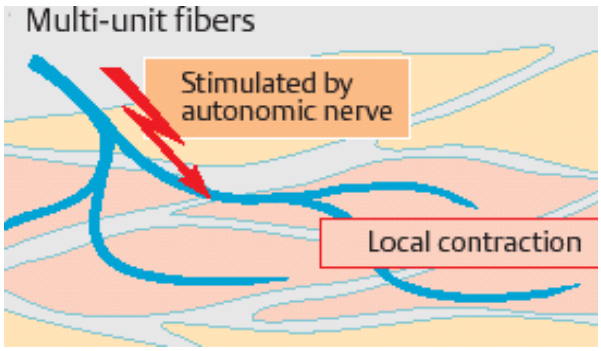
**Cell**s:

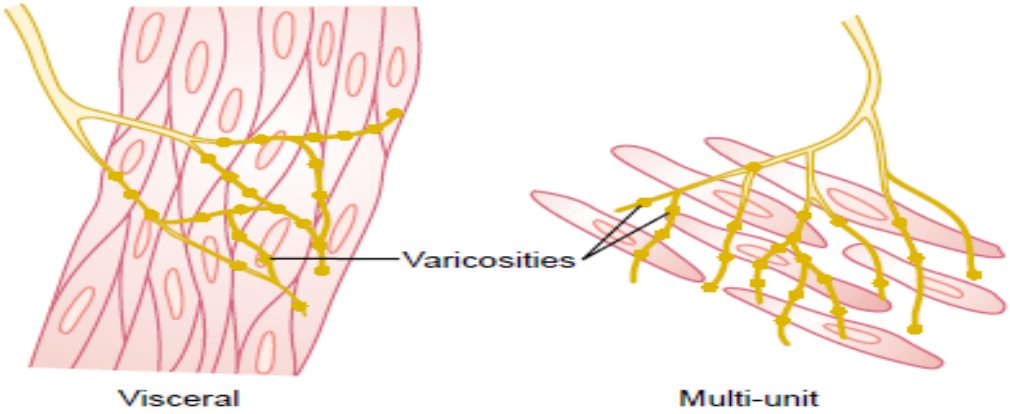
- They are isolated from one another → **does not** obey the "*all or none law*".
- They have stable RMP and do not show spontaneous pacemaker activity.

**Contraction**:

- Each fiber contracts independently & separately.
- They are dependent on autonomic nerve supply for contraction (= neurogenic).



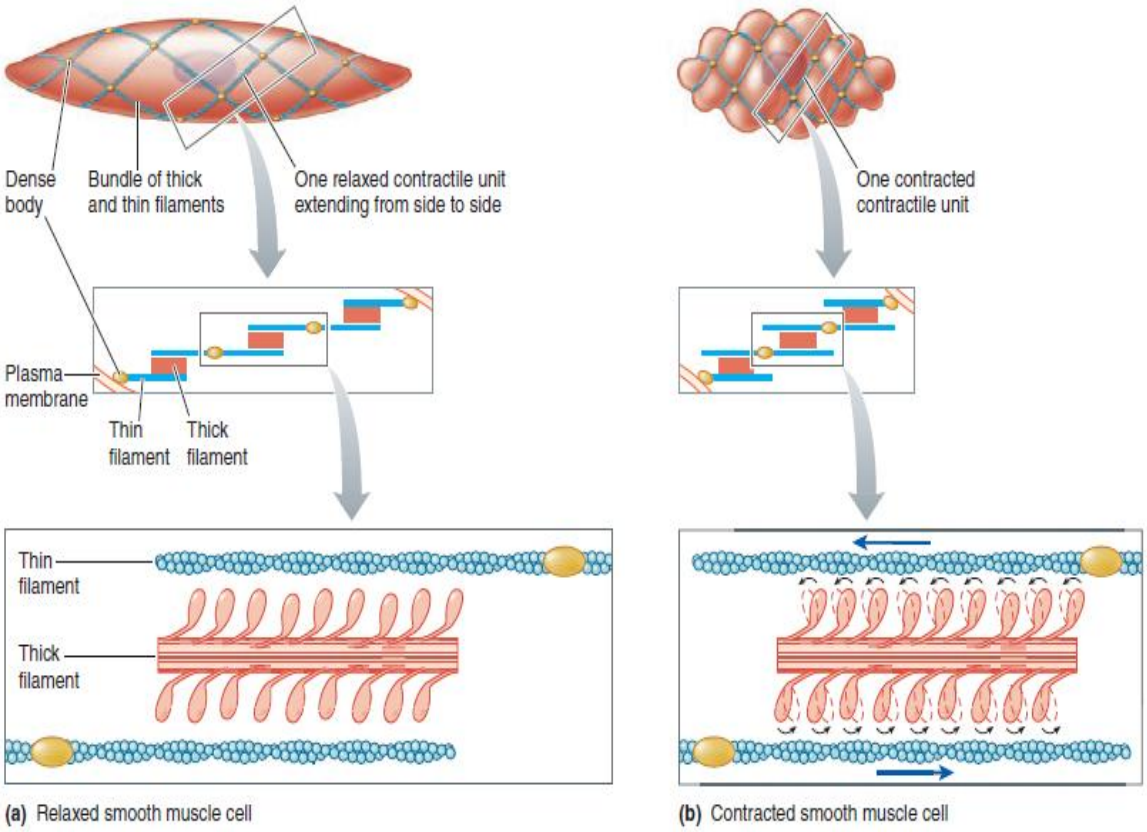



## Mechanism of Smooth Muscle Contraction:

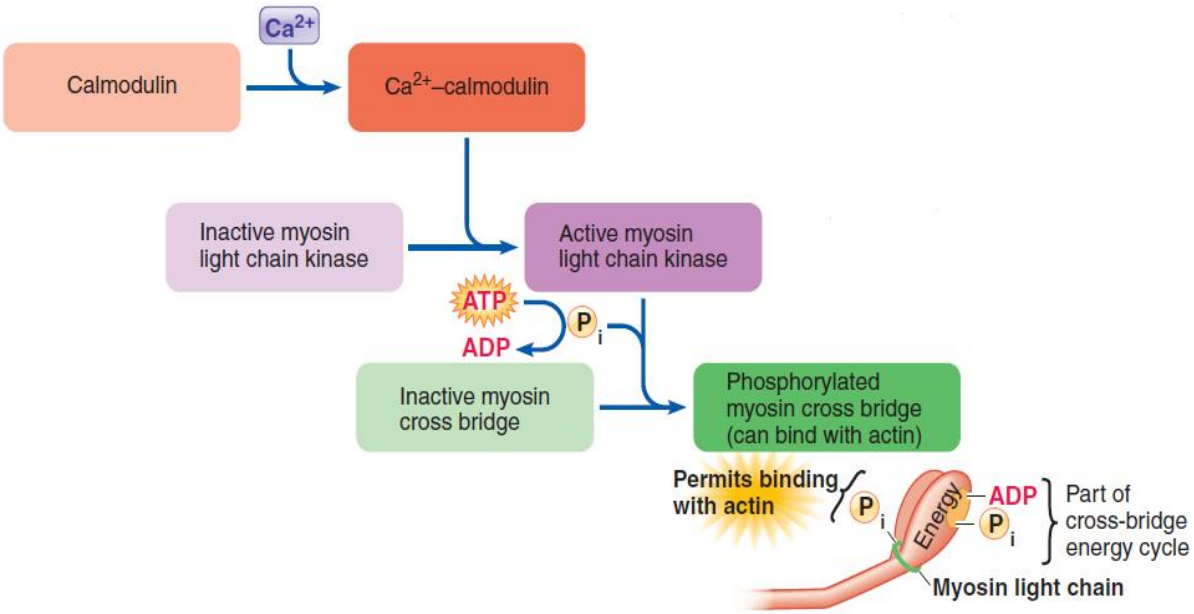
- The thin filaments of smooth muscle cells do not contain troponin, and tropomyosin does not block actin's cross-bridge binding sites. What, then, prevents actin and myosin from binding at the cross bridges in the resting state, and how is cross-bridge activity switched on in the excited state?
- Lightweight chains of proteins are attached like "necklaces" to the heads of myosin molecules, near the "neck" region.
- These so-called light chains have a crucial regulatory function in smooth muscle.
- Smooth muscle myosin can interact with actin only when the light chain is phosphorylated (that is, has an inorganic phosphate from ATP attached to it).

Steps of smooth muscle contraction:

- Calcium influx into the cytoplasm
  - Mainly (90%) from ECF [via voltage-gated calcium channel & ligand-gated calcium channels]
  - And only (10%) from the poorly developed SR.
- ↑ Cytoplasmic $Ca^{++}$ concentration.
- Calcium binds to calmodulin.
- Formation of calcium – calmodulin complex.
- Activation of calmodulin – dependent myosin light chain kinase enzyme (MLCK) of the thick filament.
- MLCK phosphorylates myosin light chains, a component of the myosin cross bridges.
- Phosphorylation allows the myosin ATPase to be activated.
- ↑ Myosin ATPase activity.
- Binding of myosin to actin.
- Cross bridge cycle formation (binding & bending & detachment) but at slower rate.
- Actin slides on myosin producing tension & shortening, but it twists in a corkscrew-like manner.



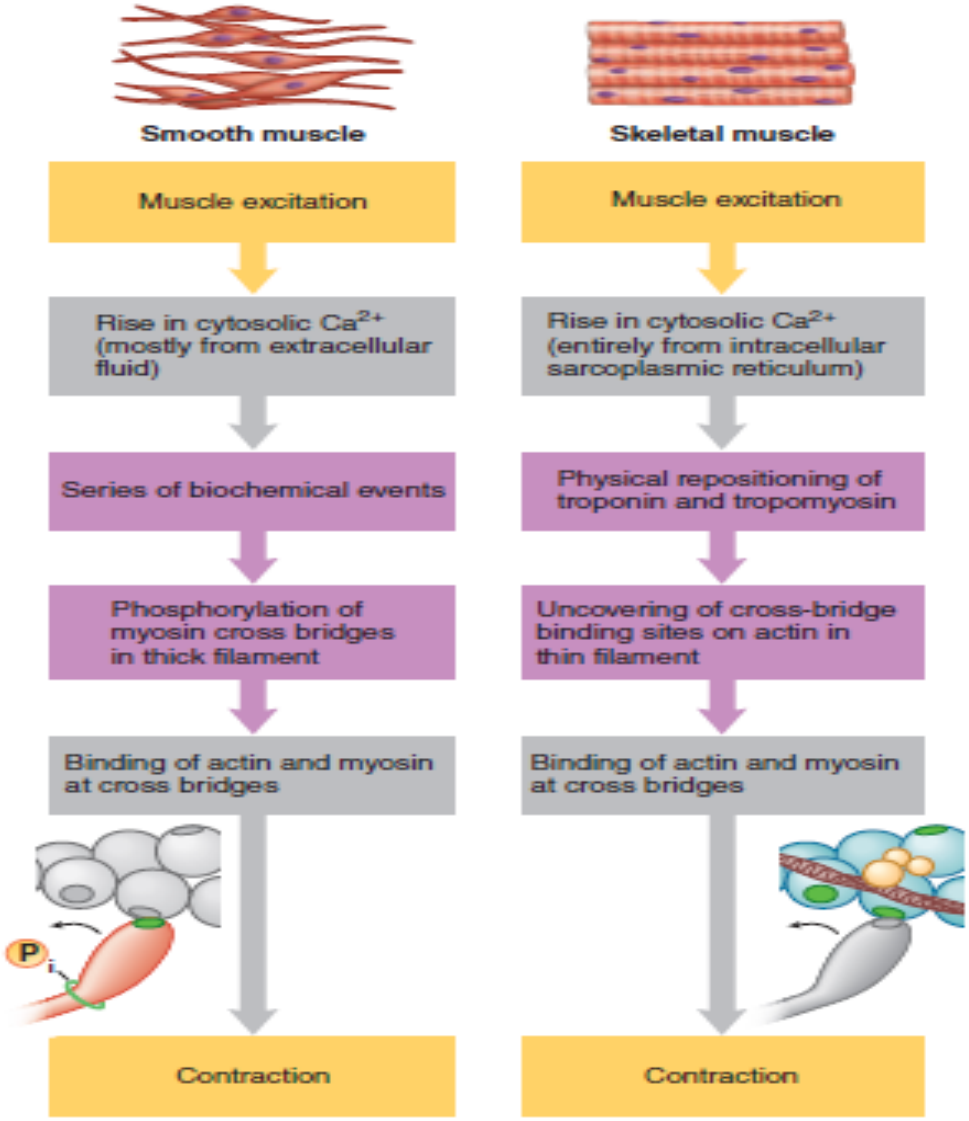

Arrangement of thick and thin filaments in a smooth muscle cell in relaxed and contracted states




Calcium activation of myosin cross-bridge in smooth muscle

☺ **N.B:**

- Therefore, smooth muscle is triggered to contract by a rise in cytosolic $Ca^{2+}$, similar to what happens in skeletal muscle.
- In smooth muscle, $Ca^{2+}$ ultimately turns on the cross bridges by inducing a *"chemical change"* in myosin in the thick filaments (phosphorylation).
- whereas in skeletal muscle it exerts its effects by causing a "*physical change*" at the thin filaments (moving troponin & tropomyosin from their blocking positions)




Comparison of the role of $Ca^{2+}$ in bringing about contraction in smooth muscle and skeletal muscle

## Mechanism of Smooth Muscle Relaxation:

Steps of smooth muscle relaxation:

- It is an active process.
- ↓ $Ca^{++}$ level in the cytoplasm to the resting level by:
  - $Ca^{++}$ pumped actively to ECF
  - $Ca^{++}$ pumped actively to SR
- De-phosphrylation of myosin light chain by myosin light chain phosphatase.
- This finally results in relaxation or sustained contraction due to latch bridge mechanism.

Latch bridge mechanism:

- Mechanism by which myosin cross-bridges remains attached to actin for some time after cytoplasmic $Ca^{++}$ concentration falls.
- This process produces sustained contraction with little energy expenditure.
- Relaxation of the muscle occurs when there is final dissociation of calcium–calmodulin complex.

## Functional Characteristics of Smooth Muscle:

1) Slow onset of contraction and relaxation:
   - The smooth muscle has a low and slow ATPase activity causing reduction of the velocity of smooth muscle contraction.
2) Slow cross bridge cycling:
   - Cross bridge cycling "bind-bend-detachment" is much slower than that of skeletal muscle.
3) Utilization of small amount of energy:
   - Total duration of contraction is about 1-3 sec. about 30 times as that of skeletal muscle.
   - As each cross bridge cycle requires one molecule of ATP regardless its duration, less energy is needed to sustain the contraction in smooth muscle.
   - Because of the low ATP utilization, the smooth muscle is fatigue resistant.
4) Latch bridge mechanism:
   - Latch bridge mechanism produces sustained contraction (prolonged tonic contraction) with very little use of energy that is especially important in vascular smooth muscles.
5) Length–tension relationship (Plasticity):
   - Another special character of smooth muscle, especially the visceral unitary type of smooth muscle of many hollow organs, is the variability of the tension it exerts at any given length.
   - If a piece of smooth muscle is stretched → $1^{st}$ it exerts increased tension.

- If it is held at the greater length → the tension gradually decreases even below the original tension.
- This property allows the hollow viscera e.g. urinary bladder to accommodate large amount of urine without much increase in their wall tension (= pressure).

6) Control of contraction:
   - Smooth muscle is highly sensitive & adapted to respond to various changes in the internal environment.
   - It could be activated by nervous signals as well as by hormones or neurotransmitters and chemical substances because the smooth muscle membrane contains many different types of receptor proteins.

   a) *Autonomic NS*:
      - Parasympathetic stimulation, acetylcholine, or other para-sympathomimetic drugs → e.g. increase motility (= contraction) of GIT wall.
      - Sympathetic stimulation, nor-epinephrine, epinephrine or other sympathomimetic drugs → e.g. decrease motility (= contraction) of GIT wall.

   b) *Hormones*:
      - Catecholamines → Produce the same effect of sympathetic stimulation, e.g. decrease motility (= contraction) of GIT wall.
      - Vasopressin (= hormone released from posterior pituitary gland → Produces contraction of the smooth muscle in the vascular wall → VC.
      - Ovarian hormones → Produce special effect on uterine muscle:
        - Estrogen: stimulate uterine contractions.
        - Progesterone: inhibit uterine muscle leading to relaxation.

   c) *Chemical Factors: (Ions, pH, Osmotic Pressure, Gases)*
      - Excess $K^+$, alkalis (↑pH), ↑$O_2$, hypotonic solutions → Increases the excitability of smooth muscle → ↑ Contraction.
      - Excess $Ca^{++}$, acids (↓pH), ↑$CO_2$, hypertonic solutions → Decreases the excitability of smooth muscle → ↓ Contraction.

   d) *Temperature:*
      - Cold → Increases the excitability of smooth muscle → ↑ Contraction.

   e) *Stretch:*
      - Stretch → Increases the excitability of smooth muscle → ↑ Contraction.

# Single-Unit Smooth Muscle

## Electrical Activity:

**R**esting **M**embrane **P**otential (RMP):

- The RMP is about −50 to −60 millivolts (mV).
- Actually, it has no true "resting" value being relatively low when tissue is active and higher when it is inhibited.

**A**ction **P**otential (AP):

- **Stimulus:**

  The action potential can be elicited for example by:

  - Electrical stimulation.
  - Action of hormones.
  - Action of transmitter substances.
  - Stretch.
  - Self-generated.

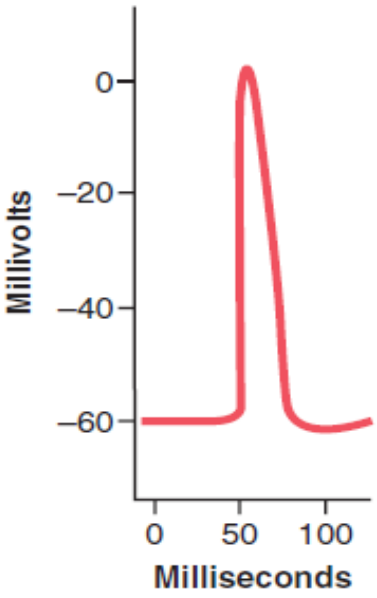
- **Mechanism:**
  - The de-polarization phase is due opening of the slow voltage-gated $Ca^{++}$ channels.
  - The re-polarization phase due to delayed activation of the voltage-gated $K^{+}$ channels.

- **Types:**

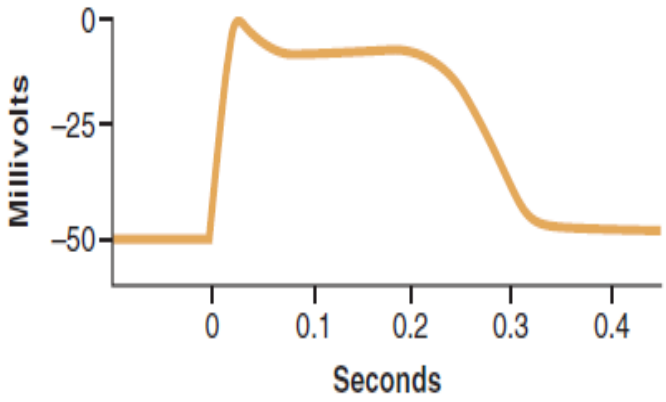
  The action potentials of visceral smooth muscle occur in one of two forms:

  (1) Spike Potentials
  - Typical spike action potentials, such as those seen in skeletal muscle.
  - Its duration 10 – 50 msec.

  (2) Action Potentials with Plateau
  - The onset of this action potential is similar to that of the typical spike potential. However, instead of rapid re-polarization of the muscle fiber membrane, the re-polarization is delayed for several hundred milliseconds.
  - Its duration ~ 300 msec.
  - The importance of the plateau is that it can account for the prolonged contraction that occurs in some types of smooth muscle, such as the uterus (during labor).




Spike potential



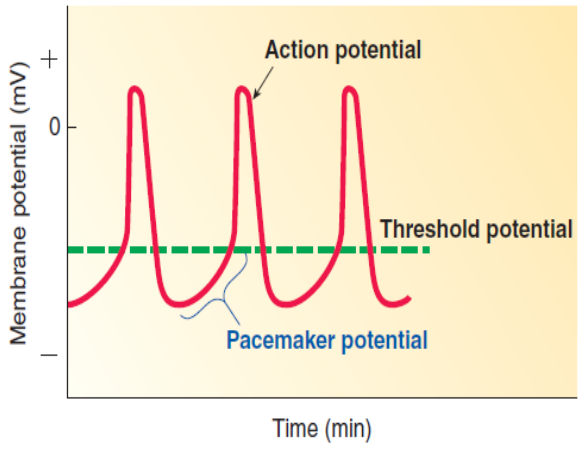

Action potential with a plateau

## Self-Generated Electrical Activity:

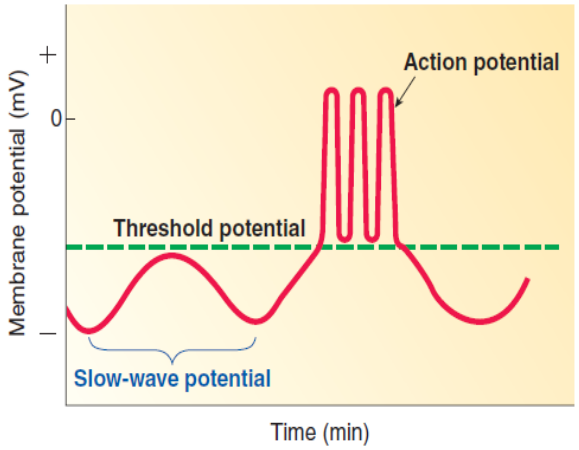
- Some smooth muscle is self-excitable.
- They are capable of initiating spontaneous electrical activity (APs) in absence of external stimulation.
- Self-excitable smooth muscle cells are specialized **only** *to initiate action potentials*, but they are not equipped to contract.
- The spontaneous production of APs makes the single-unit smooth muscle cells capable of contraction without need for nerve supply (= myogenic activity).
- Spontaneous de-polarizations displayed by self-excitable cells are of two forms:
  (1) Pacemaker Potentials
    - The membrane potential of some smooth muscle cells gradually depolarizes on its own.
    - When the membrane has depolarized to threshold, an action potential is initiated.
    - After re-polarizing, the membrane potential again depolarizes to threshold, cyclically continuing in this manner to repetitively self-generate action potentials.
    - These smooth muscle cells which spontaneously depolarize; are called pacemaker cells.
    - These pacemaker cells have pre-potential activity of slow spontaneous de-polarization due to decreased $K^+$ permeability and increased $Ca^{++}$ and $Na^+$ permeabilities.

(2) Slow-Wave Potentials

- In some smooth muscle cells, there are spontaneous, regular, repetitive oscillations of the membrane potential (slow waves).
- When the amplitude of the slow waves is sufficient enough to depolarize the cell to the threshold, the resulting action potential lead to more $Ca^{++}$ influx and phasic contractions.




Pacemaker potential




slow-wave potential

## Mechanical Activity:

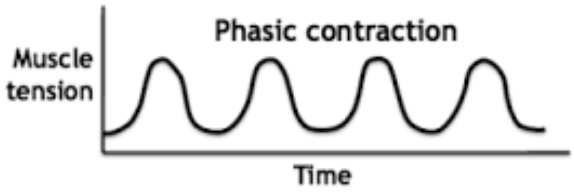
The mechanical activity (= muscle contraction) could be manifested as:

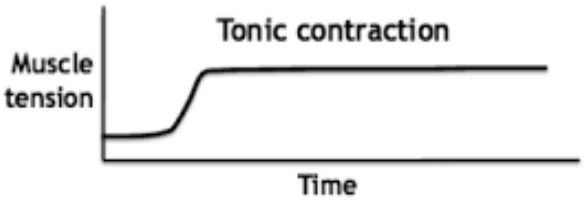
(1) Phasic activity

- This activity is composed of rhythmic contractions and relaxations.
- It takes the form of propulsive movements.
- So, this type of movement allows propulsion of the lumen content in one direction

(2) Tonic activity

- Tonus = tone = maintained state of partial contraction.
- Smooth muscle can maintain a state of long-term steady contraction.
- This type of tonic contractions resists the continuous distending forces by the content of the visceral lumen.
- It is best seen in the sphincters of the gut and urinary bladder and in the tone of the blood vessels.




# Multi-Unit Smooth Muscle

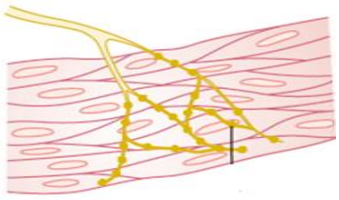
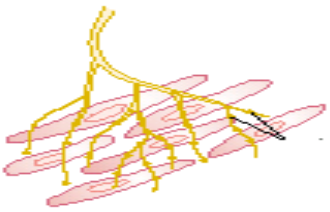
## Electrical Activity:

- The RMP is stable and does not show spontaneous pacemaker activity.
- No gap junctions between the cells → it **does not** obey the "*all or none law*".
- No self-generated electrical activity.

## Mechanical Activity:

- Contraction is only phasic when stimulated by nerves.

## Comparison between Single-unit & Multi-unit Smooth Muscles

| | **Single-unit** | **Multi-unit** |
|---|---|---|
| |  |  |
| **Site** | In the wall of hollow visceral organs (GIT, uterus, urinary bladder) | - Ciliary muscle & iris of the eye<br>- Piloerector muscle of the hair |
| **Cells** | - Connected by gap junctions<br>- Electrically coupled<br>- Syncytial smooth muscle | Isolated from one another |
| **Electrical Activity** | - Unstable RMP<br>- Spontaneous electric activity<br>- Slow waves superimposed by spike potential or pace maker potential | - Stable RMP<br>- No spontaneous electric activity<br>- Excitations are produced only upon nerve stimulation |
| **Rhythm** | Rhythmic | Non-rhythmic |

| | | |
|---|---|---|
| **Mechanical Activity** | - Spontaneous contractions<br>- Fibers act as one single unit<br>- Obey all or none law<br>- Phasic or tonic | - Do not spontaneously contract<br>- Fibers contract independently, separately<br>- Does not obey all or none law<br>- Phasic activity only |
| **Control** | Myogenic<br>- Modulated by both ANS & humoral Fs<br>- More sensitive to stretch | Neurogenic<br>- Modulated by humoral factors<br>- Less sensitive to stretch |

## References:

1. Guyton and Hall
   Text book of Medical Physiology, 13th Edition, Chapter 8 (**Excitation and Contraction of Smooth Muscle**)

2. Ganong's
   Review of Medical Physiology, 24rd Edition, Chapter 5 (**Excitable Tissue: Muscle**), Page: 114 – 116

3. Fox
   Human Physiology, 14th Edition, Chapter 12 (**Muscle: Mechanisms of Contraction and Neural Control**), Page: 393– 397

4. Sherwood:
   Human Physiology: From Cells to System, 9th Edition, Chapter 8 (**Muscle Physiology**), Page: 286– 294